

WHAT IS CLAIMED IS:

1. A reagent for measuring target analytes in a test sample, said reagent comprising at least one type of analyte sensor particle selected from each of the following classes (a) and

(b):

5 (a) ion-sensors comprising a plurality of sample-insoluble particles having associated therewith a target ionophore adapted to interact with a target ion in the sample, and a first emitted fluorescent signal following interaction of the target ionophore with a target ion;

(b) metabolite-sensors comprising a plurality of sample-insoluble particles having associated therewith a ligand adapted to interact with a target metabolite in the sample to produce a second fluorescent signal following interaction of the ligand with the target metabolite;

and at least one type of analyte sensor particle selected from the following classes (c), (d) and

(e):

15 (c) enzyme-sensors comprising a plurality of sample-insoluble particles having associated therewith a fluorogenic substrate adapted to interact with a target enzyme in the sample to produce a third fluorescent signal;

20 (d) antigen- or antibody-sensors comprising a plurality of sample-insoluble particles having associated therewith an immobilized pair member adapted to interact to form a complex with a complementary target antigen or a complementary antibody and to produce a fourth fluorescent signal following interaction of the pair member with the complementary target antigen or complementary antibody; and

25 (e) nucleotide sequence-sensors comprising a plurality of sample-insoluble particles having associated therewith a polynucleotide molecule complementary to a target nucleotide sequence and capable of hybridizing with the target nucleotide

sequence under hybridizing conditions, and a fluorescent signal material that produces a fifth fluorescent signal upon hybridization between the complementary polynucleotide molecule and the target nucleotide sequence;  
wherein the reagent mixture includes sensor particles which interact specifically with

5 each of the following analytes:

(A) at least one analyte selected from the group consisting of alkali metal ions, alkaline earth metal ions, ammonium, halide ions, oxygen, pH, carbon dioxide;

(B) at least one analyte selected from the group consisting of saccharides, ammonia, urea, uric acid, cholesterol, triglycerides, ethanol, lactate, salicylate, acetaminophen, bilirubin and creatinine; enzymes, antibodies, antigens and polynucleotide sequences.

2. A reagent according to claim 1, wherein said alkali metal ions are selected from the group consisting of ions of sodium and potassium; said alkaline earth metal ions are selected from the group consisting of ions of calcium and magnesium; and said halide ions are chloride ions.

3. A reagent according to claim 1, wherein said saccharides are selected from the group consisting of glucose, fructose, lactose and galactose.

4. A reagent according to claim 1, wherein said enzymes are selected from the group consisting of alkaline phosphatase, alanine aminotransferase, aspartate aminotransferase, amylase, cholinesterase, creatine kinase, gamma-glutamyl transferase, lactate dehydrogenase and lipase.

20 5. A reagent according to claim 1, wherein said sensor particles have a size in the range from about 0.1  $\mu\text{m}$  to about 50  $\mu\text{m}$ .

6. A reagent according to claim 1, which comprises at least one type of analyte  
25 sensor particle selected from each of the classes (a), (b) and (c).

7. A reagent according to claim 1, which comprises at least one type of analyte sensor particle selected from each of the classes (a), (b) and (d).

8. A reagent according to claim 1, which comprises at least one type of analyte sensor particle selected from each of the classes (a), (b) and (e).

5 9. A reagent according to claim 1, which comprises at least one type of analyte sensor particle selected from each of the classes (a), (b), (c) and (d).

10. A reagent according to claim 1, which comprises at least one type of analyte sensor particle selected from each of the classes (a), (b), (c) and (e).

11. A reagent according to claim 1, which comprises at least one type of analyte sensor particle selected from each of the classes (a), (b), (d) and (e).

12. A reagent according to claim 1, which comprises at least one type of analyte sensor particle selected from each of the classes (a), (b), (c), (d) and (e).

13. A method for assaying multiple analytes in a test sample, said method comprising the steps of:

20 (1) admixing a test sample containing multiple analytes to be measured with a reagent mixture comprising a plurality of types of sensor particles, each type of sensor particle comprising coding indicia which confer uniquely identifying optical properties on that type of particle and a measurement substrate which specifically interacts with an analyte of interest such that measurement optical properties of said substrate are varied, said reagent mixture including particles which interact specifically with each of the following analytes:

(A) at least one analyte selected from the group consisting of alkali metal ions, alkaline earth metal ions, ammonium, halide ions, oxygen, pH, carbon dioxide;

(B) at least one analyte selected from the group consisting of saccharides, ammonia, urea, uric acid, cholesterol, triglycerides, ethanol, lactate, salicylate, acetaminophen, bilirubin and creatinine;

5 (C) at least one analyte selected from the group consisting of enzymes, antibodies, antigens, and polynucleotide sequences,

(2) allowing the resulting admixture to incubate for a period of time sufficient for each type of sensor particle to interact with the analyte with which it specifically interacts to vary the measurement optical properties of the sensor particle;

(3) transferring the admixture to a reading device and reading both the coding and the measurement optical properties of each sensor particle individually;

(4) storing the measured optical properties of each sensor particle type according to the coding optical properties read from the particles; and

(5) processing the stored measurements for each sensor particle type to obtain an assay result for the analyte associated with each type of sensor particle;

whereby a complete chemical analysis of the test sample is obtained.

14. A method according to claim 13, wherein said alkali metal ions are selected from the group consisting of ions of sodium and potassium; said alkaline earth metal ions are selected from the group consisting of ions of calcium and magnesium; and said halide ions are chloride ions.

20 15. A method according to claim 13, wherein said saccharides are selected from the group consisting of glucose, fructose, lactose and galactose.

16. A method according to claim 13, wherein said enzymes are selected from the group consisting of alkaline phosphatase, alanine aminotransferase, aspartate aminotransferase, amylase, cholinesterase, creatine kinase, gamma-glutamyl transferase, lactate dehydrogenase and lipase.

17. A method according to claim 13, wherein said reading device is a flow cytometer, said measurement optical properties of said particles are fluorescence, and said reading step is carried out by measuring the fluorescence of each type of sensor particle.

18. A kit comprising

5 an apparatus for assaying multiple analytes in a test sample, and instructions for use of the apparatus setting forth the method of Claim 13.

19. An apparatus for assaying multiple analytes in a test sample, said apparatus comprising:

(A) an inlet for a test sample which is to be analyzed;

(B) an inlet for a reagent mixture containing a plurality of types of sensor particles, each type of sensor particle being designed to specifically interact with an analyte of interest to vary the optical properties of an associated fluorescent indicator;

(C) an incubation chamber or vessel in which the sample and reagent mixture are allowed to interact;

(D) a flow cytometer read cell adapted to read coding indicia on each sensor particle passed through the cell to identify the type of sensor particle and the analyte of interest with which the particle interacts, and to read the associated fluorescent indicator to obtain a measured value indicative of whether the sensor particle has interacted with the respective analyte of interest; and

20 (E) a controller adapted to store measured values read for each sensor particle according to the type of sensor particle and the specific analyte with which that type of sensor particle interacts, and to process the stored measured values for each sensor particle type to obtain an assay result for the analyte associated with each type of sensor particle.

20. An apparatus according to Claim 19, wherein said flow cytometer read cell

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(A) a first diode laser for exciting a bead label of each bead to emit an identifying fluorescent signal and a first photodetector for detecting the identifying fluorescent signal; and

(B) a second laser diode for exciting the fluorescent indicator associated with each bead to emit a measurement signal and a second photodetector for detecting the measurement signal;

wherein said measurement signal is in the near-infrared wavelength range.

21. An apparatus for assaying multiple analytes in a test sample, said apparatus comprising:

- (A) means for introducing a test sample which is to be analyzed;
- (B) means for introducing a reagent mixture containing a plurality of types of sensor particles, each type of sensor particle being designed to specifically interact with an analyte of interest to vary the optical properties of an associated fluorescent indicator;
- (C) an incubation chamber or vessel in which the sample and reagent mixture are allowed to interact;
- (D) a flow cytometer read cell adapted to read coding indicia on each sensor particle passed through the cell to identify the type of sensor particle and the analyte of interest with which the particle interacts, and to read the associated fluorescent indicator to obtain a measured value indicative of whether the sensor particle has interacted with the respective analyte of interest; and

(E) a controller adapted to store measured values read for each sensor particle according to the type of sensor particle and the specific analyte with which that type of sensor particle interacts, and to process the stored measured values for each sensor particle type to obtain an assay result for the analyte associated with each type of sensor particle.